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　　サブミリの空間分解能での機能的磁気共鳴脳活動イメージング
２．研究機関：
　　理化学研究所脳科学総合研究センター
３．研究者名と所属 ：
　　程康（Kang Cheng）（科学技術振興事業団／理化学研究所脳科学総合研究センター）
４．研究協力者名と所属：
　　R. Allen Waggoner（科学技術振興事業団／理化学研究所脳科学総合研究センター）
　　田中啓治（理化学研究所脳科学総合研究センター）
５．研究期間：1998 年－2000 年

６．要約

　第一次視覚野では、左目あるいは右目から強い入力を受ける神経細胞がそれぞれ固まって存在し、周期的に交互に並んだ帯状の領域（眼優位性コラムと呼ばれる）を構成することが知られている。眼優位性コラムは機能的磁気共鳴画像(fMRI)の空間分解能の限界を調べるために理想的なモデル系である。私たちは４テスラの静磁場の MR 装置を用いて、分割 EPI 法（画像構成法の一種）により健常な被験者の第一次視覚野の眼優位性コラムを画像化（イメージング）することを試みた。第一次視覚野が比較的平らに広がった鳥矩溝の上壁に平行になるようにスライスを設定し、使用する視覚刺激で刺激される第一次視覚野の範囲を予め別の実験により定め、この範囲で左目刺激と右目刺激で信号の大きさが一貫して変化する画素の分布を調べた。左目優位の画素と右目優位の画素は約１ミリの間隔で交互に並んだ帯状の領域に固まって存在した。帯の方向と間隔は、片目を治療目的で摘出した患者の死後脳をチトクローム酸化酵素に対する組織化学的方法で染色することによって調べられた眼優位性コラムのデータ(Horton et al., 1990)とよく一致した。また、同じ被験者のほぼ同じスライス部位について別の日に行った fMRI 実験において、よく重複する眼優位性コラムのパターンが再現された。これらの私たちの結果は、高静磁場 fMRI を使って人間の脳機能を 1 ミリ以下の高空間分解能で研究できることを示した。

７．研究目的

In the primary visual cortex (V1), neurons located in, (and to lesser extent) above and below layer IVc are primarily driven by inputs from the left or the right eye, and are organized in periodic left-right alternating stripes known as ocular dominance columns (ODCs). In humans, ODCs have been revealed by applying cytochrome oxidase stain to the brains obtained after death from patients who had undergone enucleation of one eye many years before death, in which the width of individual columns is estimated about 0.5-1 mm [1]. Although it has been shown that ODCs can be resolved using high-field fMRI [2, 3], the issue regarding spatial properties of ODC patterns as revealed by fMRI has not been sufficiently addressed. In this study, we have attempted 1) to reveal and analyze ODC patterns in anatomically well-defined sections of V1 under various conditions, and 2) to reproduce ODC patterns over different experiments using high-field (4 T) fMRI.

８．材料と方法

Two healthy male subjects participated in repeated experiments conducted on a Varian Unity Inova 4 T whole-body MRI system equipped with a Magnex head gradient system. A 3” single-loop surface coil was used for high-resolution functional and anatomical scans around V1. All images were collected with a FOV of 24x24 cm^2 and a matrix of 512x512 pixels (in-plane resolution=0.47x0.47 mm^2). Functional images were acquired using segmented (32 segments) GRE-EPI with segments between slices (3 slices, thickness=3mm) interleaved (volume TR=300ms, TE=15ms, FA=40°).

The three slices covering the dorsal V1 were determined after vertical meridian representation (defining V1/V2 border) and retinotopy in V1 were mapped in separate experiments. The slices, parallel to the calcarine sulcus (CS) (ODCs roughly run parallel to CS), were prescribed on high-resolution parasagittal FLASH anatomical images (thickness=3mm) collected at the beginning of each experiment, and could be well re-positioned across experimental sessions. Visual stimuli were delivered to the subject’s eyes via a pair of Avotec optic fiber bundles. Prolonged stimulation with an 8 Hz reversing black/white checkerboard (30°x23°) was applied to the left eye (L) or the right eye (R), separated by dark presentation to both eyes (D), while subjects maintained fixation. In total, 150 (3-slice) volumes of functional images were acquired each time in about 24 minutes.

After EPI images were reconstructed, cardiac and respiratory noises were removed [4]. Images were then registered [5], and the system drifts were removed with a band-pass filter.

Statistical t-maps were generated using STIMULATE [6] for comparisons of L>D, R>D, L>R, and R>L, respectively. L>D and R>D maps ($P<0.01$, signal change <5%) served as masks limiting activated pixels within the brain tissue. Within activated portion of V1, ODC maps were generated for pixels responding preferentially to the left (L>D and L>R) and right (R>D and R>L) eye stimulation at multiple thresholds.

９．結果

In general, responses to prolonged stimulation to the left or the right eye could be differentiated at all thresholds with different number of pixels showing differential responses at each threshold. Left-right alternating ODC-like patterns could be reliably identified in less curved/sulcated sections of V1. In one subject with a flat CS on the right hemisphere, ODC-like patterns were best observed on a slice containing the upper bank of the right CS representing 2.5-10° eccentricity, where they appeared orthogonal to the pia. The mean width of mapped ODCs estimated by measuring center-to-center distances between neighboring columns was about 1.1 mm. These observations conform to the findings reported by Horton et al. [1]. ODC-like patterns on the slices covering the medial wall of V1, where real ODCs intersect the scanning slices, appeared wider. This is expected, as predicted by simulations, if real ODCs are not truly perpendicular to the scanning slices.

In repeated experiments on the same subjects, it was shown that ODC-like patterns could be largely reproduced in different experiments, either within the same experimental session or over different experimental sessions.

10. 考察

We have shown that responses to prolonged monocular stimulation could be differentiated. Left-right alternating ODC-like patterns could be observed in anatomically well-defined section of V1. We also showed that mapped ODC patterns could be largely reproduced, either within the same experimental session, or over different sessions. Taken together, these results demonstrated that with careful experimental procedure, it is possible to resolve human ODCs using high-field fMRI. However, as the appearance of mapped ODCs are influenced by the morphology of mapped V1, and only a small portion of V1 can be mapped at a time, it has not been possible to reconstruct the whole human ODCs using fMRI. At this point we should be cautious in interpreting and quantitating these results.

11. 今後の展開

It is hoped that the experiences that we accumulated in this work will eventually help us in the future explore functional structures and modules in high brain areas.

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14. Imaging Brain Activity with fMRI at Sub-millimeter Spatial Resolution
15. RIKEN Brain Science Institute
16. Kang Cheng (JST and RIEKN Brain Science Institute)
17. R. Allen Waggoner (JST and RIEKN Brain Science Institute)
Keiji Tanaka (RIEKN Brain Science Institute)
18. 1998-2000

19. Abstract

In the primary visual cortex (V1), neurons located in, (and to lesser extent) above and below layer IVc are primarily driven by inputs from either the left or the right eye, and are organized in periodic left-right alternating stripes known as ocular dominance columns (ODCs). ODC provides an ideal model for testing the capability of functional magnetic resonance imaging (fMRI) at high spatial resolution. We have attempted to map ODCs in normal human subjects using high-field (4T) fMRI with a segmented EPI technique. The differential responses to the left- or the right-eye stimulation could be reliably resolved in anatomically well defined sections of V1. The patterns of revealed ODCs conformed to those studied with cytochrome oxidase stain applied to the brains obtained after death from patients who had undergone enucleation of one eye many years before death (Horton et al., 1990). In addition, we showed that mapped ODC patterns could be largely reproduced in different experiments

conducted either within the same experimental session or over different sessions. Our results demonstrate that high-field fMRI can be used for studying functions of living human brains at higher (< 1 mm) spatial resolution.